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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,280	09/30/2003	Timothy R. Billiar	14022-011001	7071

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
08/19/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/676,280	BILLIAR ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,21-40 and 55-73* is/are pending in the application.

4a) Of the above claim(s) *4-9 and 21-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10,11 and 55-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/4/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner acknowledges receipt of request for extension of time, IDS, amendment and remarks filed 6/04/2010. Claim 1 is amended. New claims 66-73 are added. Therefore claims 1-11, 21-40 and 55-73 are pending and of these claims 4-9 and 21-40 are withdrawn form consideration.

Response to Arguments

2. The rejections that are not reiterated herein are withdrawn. For example, the amendment to claim 1 reciting the concentration of CO in the composition administered overcomes the scope of enablement rejection.

3. The amendment to claim 1 and the presentation of new claims 66-73 gives rise to the new rejections below using the art of record.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 3, 55 and 56 and new claims 66-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujita et al. ("Paradoxical rescue from ischemic lung injury by inhaled carbon monoxide driven by depression fibrinolysis," Nature Medicine, 7, 598-604, 2001) or Pinsky et al. (US 2005/0048133 A1) in view of Carceller et al. (US 5,420,131) or Neely (US 5,504,090) and further in view of Bach et al. (US 2003/0039638).

7. Fujita discloses that inhaled CO protects against ischemic lung tissue injury (see the whole document with emphasis on the abstract; page 601, left column, three lines from the bottom). Fujita uses CO composition that is blended with room air and the air blended with room air is administered by inhalation (page 602, right column 4th full paragraph). The CO blended with room air meets the composition of claim 1 and inhalation meets claim 3.

8. Fujita teaches treating ischemic injury. Fujita does not teach treating hemorrhagic shock. But, ischemia and hemorrhagic shock have been known to be treated by the same compositions. For example, Neely teaches method of treating ischemia and reperfusion, sepsis, anaphylaxis, hemorrhagic shock and trauma in patients in need thereof with the inventive composition of Neely (see column 6, lines 24-29). Also, Carceller treats septic shock, anaphylactic shock, hemorrhagic shock and myocardial ischemia in a mammal in need thereof by administering an effective amount of the compound of Carceller (see claim 13).

9. Therefore, the teaching of Fujita and Carceller or Neely, can be combined by a person of ordinary skill in the art at the time the invention was made in order to administer a composition comprising CO to a mammal/subject in need thereof with the expectation of effectively treating ischemic injuries or hemorrhagic shock since these conditions have been known to be treatable by the same compositions or compounds.

10. Pinsky teaches method of treating ischemic disorder in a subject in need thereof by administering carbon monoxide gas or mixture of CO and inert gases such as air, oxygen, nitrogen and argon in sufficient amount over sufficient period of time (paragraphs [0055], [0056], [0057], [0058]-[0061]) by inhalation or by extracorporeal exposure to blood or body fluids. The CO mixed with the inert gases meets the limitation of the composition of claim 1. Administration by inhalation meets the administration of claim 1 and administration by inhalation of claim 3.

11. Pinsky teaches treating ischemic injury. Pinsky does not teach treating hemorrhagic shock. But, ischemia and hemorrhagic shock have been known to be treated by the same compositions. For example, Neely teaches method of treating ischemia and reperfusion, sepsis, anaphylaxis, hemorrhagic shock and trauma in patients in need thereof with the inventive composition of Neely (see column 6, lines 24-29). Also, Carceller treats septic shock, anaphylactic shock, hemorrhagic shock and myocardial ischemia in a mammal in need thereof by administering an effective amount of the compound of Carceller (see claim 13).

12. Therefore, the teaching of Pinsky and Carceller or Neely, can be combined by a person of ordinary skill in the art at the time the invention was made in order to administer a composition comprising CO to a mammal/subject in need thereof with the expectation of effectively treating

ischemic injuries or hemorrhagic shock since these conditions have been known to be treatable by the same compositions or compounds.

13. Pinsky describes exposing the subject to the CO for 12 hours (see paragraph [0028], [0058]) so that with respect to claim 56, the artisan would be motivated to expose the subject to the CO that would produce the goal of treating the ischemia or hemorrhagic shock since same compositions have been known to treat ischemic conditions and hemorrhagic shock.

14. However, while Fujita or Pinsky can be combined with Carceller or Neely in order to administer composition containing CO to a mammal and expect to effectively treat ischemic injuries or hemorrhagic shock since these conditions have been known to be treatable by the same compounds or compositions (see at least claim 13 of Carceller and Neely at column 6, lines 24-29), Fujita or Pinsky does not teach the ppm concentration of the CO now recited in claim 1.

15. But, Bach teaches that a subject in need thereof is exposed to levels of CO at 250 ppm (see paragraphs [0007], [0061], [0102], [0107], [0118], [0243] and [0265]) to treat ischemic conditions. Therefore, taking the teachings of Fujita or Pinsky in view of Carceller or Neely, and the suggestion by Bach to maintain the CO at level of 250 ppm, one having ordinary skill in the art at the time the invention was made would reasonably expect that exposure of the subject to CO at 250 ppm would be effective in treating ischemia or hemorrhagic shock.

16. The range of CO at about 10 ppm to about 3,000 ppm is generic to the disclosed concentration of 250 ppm found in Bach. Therefore, the 250 ppm, A species of the broad range of 10-3,000 ppm meets the limitation of the CO concentration in claim 1 and also meets the

limitation of the Co concentration in claims 55, 68 and 70-73 with the concentration in claims 70-73 being generic to 250 ppm.

17. Bach also discloses that amount of CO administered can vary from 0.0000001% to about 0.3%, which is from about 0.001 ppm to 3,000 ppm; Bach further disclosed that the preferred amount of CO is "at least about 0.001%, e.g., at least about 0.005%, 0.01%, 0.02%, 0.025%, 0.03%, 0.04%, 0.05%, 0.06%, 0.08%, 0.10%, 0.15%, 0.20%, 0.22%, or 0.24% by weight," and the "preferred ranges of carbon monoxide include about 0.001% to about 0.24%, about 0.005% to about 0.22%, about 0.010% to about 0.20%, and about 0.015% to about 0.1% by weight" (paragraph [0105]). From these amounts, it could be seen that 50 ppm as recited in claim 66 would be met when a 0.005% Co is used, for claim 67, the recited amount of 100 ppm would be met when 0.01% CO is used, and for claim 69, the recited amount of 500 ppm would be met when a 0.05% CO is administered.

18. Claims 1, 2, 10, 11 and 57-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujita et al. ("Paradoxical rescue from ischemic lung injury by inhaled carbon monoxide driven by depression fibrinolysis," Nature Medicine, 7, 598-604, 2001) or Pinsky et al. (US 2005/0048133 A1) in view of Carceller et al. (US 5,420,131) or Neely (US 5,504,090) and further in view of Bach et al. (US 2003/0039638) and Peitzman et al. ("Hemorrhagic shock" in Curr Probl Surg. 1995 Nov. 32 (11): 925-1002, abstract).

19. Fujita or Pinsky in view of Carceller or Neely (US 5,504,090) and further in view of Bach has been described above to render claim 1 obvious.

20. Fujita and Pinsky in view of Carceller or Neely and further in view of Bach does not teach further transfusion of blood to treat the ischemic condition in addition to the CO as described in claim 2.

21. However, Peitzman teaches that transfusion of blood is effective to treat hemorrhagic shock including ischemia; Peitzman is clear that treatment and evaluation must be simultaneous to evaluate organ and organ response, tissue damage, etc; blood circulation must be restored in which adequate red blood cell mass with its oxygen carrying capacity must be restored (see page 981, beginning at the 3rd full paragraph under treatment of hemorrhagic shock to paragraph bridging pages 983 and 984). Peitzman's critical evaluation and assessment of the condition meets claims 10 and 11. The transfusion meets claims 2 and 57 and blood transfused contains whole blood, red blood cells, platelets, plasma and coagulation factors since these are all components of blood so that claims 58-65 are met. Therefore, taking the combined teachings of Fujita, Pinsky, Carceller, Neely and Peitzman, one having ordinary skill in the art at the time the invention was made, would have reasonable expectation of success that combining blood transfusion with CO administration would effectively treat ischemia and/or hemorrhagic shock.

Response to Arguments

22. Because the rejections have been modified to address the amendment to claim 1 and the presentation of new claims 66-73, the applicant's arguments are addressed as the arguments relate to the current rejections.

23. Applicant's arguments filed 06/04/10 have been fully considered but they are not persuasive.

24. Applicant disagrees with the rejections employing Carceller and Neely because Neely and Carceller use compounds that are not carbon monoxide and since there is/are no structural similarities of the compounds of Neely and Carceller and carbon monoxide, applicant contends that the ordinary skilled artisan would not have been motivated to treat hemorrhagic shock based on Fujita, Pinsky, Carceller and Neely.

25. Response: The examiner agrees with applicant that the compounds in Neely and Carceller are not carbon monoxide. Carceller and Neely are relied upon to show that ischemic injuries and hemorrhagic shock are known to be treated by the same compounds, that is, Carceller uses its compound to treat both ischemic injuries and hemorrhagic shock and Neely uses its composition to treat both ischemic injuries and hemorrhagic shock. Therefore, based on these teachings, Carceller and Neely, the ordinary skilled artisan would be motivated to treat hemorrhagic shock and ischemic injuries with carbon monoxide following the teachings of Fujita and Pinsky and expect to effectively treat both conditions, hemorrhagic shock and ischemic injuries and in the present case, therefore, treating hemorrhagic shock with CO is prima facie obvious from the teachings of the prior art.

26. Applicant argues that Peitzman does not remedy the deficiencies of Fujita, Pinsky, Carceller and Neely because Peitzman does not teach the use of Co for treatment of hemorrhagic shock so that applicant says that the claims are patentable over Fujita or Pinsky in combination with Carceller, Neely and Peitzman.

27. Response: While it is true that Peitzman does not use CO to treat hemorrhagic shock, the examiner disagrees with applicant that Peitzman does not remedy the deficiencies of Fujita, Pinsky, Carceller and Neely because Peitzman is relied upon for the teaching of blood transfusion recited in claim 2 that is further to the method of claim 1. Therefore, with respect to claims 2 and 57-65, Peitzman remedies the deficiencies of Fujita and Pinsky in combination with Carceller and Neely.

28. Applicant also argues that Back, though relied upon to teach 250 ppm CO, does not remedy the deficiencies of Fujita, Pinsky, Carceller and Neely.

29. Response: The examiner disagrees because as noted by applicant Bach is relied upon to teach the %amount of CO needed to treat ischemic injuries/conditions and claim 55 recites 250 ppm amount of CO; Fujita and Pinsky do not disclose amounts of CO used and Bach provides that teaching that certain amounts of CO are used in the treatment of ischemic conditions. Therefore, with respect to claims 55 and 56, Bach remedies the deficiencies of Fujita, Pinsky, Carceller and Neely.

30. No claim is allowed.

31. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

32. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on Monday to Thursday from 7 a.m. to 5:30 p.m.

34. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

35. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Primary Examiner, Art Unit 1618